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EXAMINER	
COLLINS, CYNTHIA E	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 03/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/938,342	INZE ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-31 and 33-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-31 and 33-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed December 8, 2003 has been entered.

Claims 1-22 and 32 are cancelled.

Claims 23-31, 33-36 and 38-39 are currently amended.

Claims 40-46 are newly added.

Claims 23-31 and 33-46 are pending and are examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All previous objections and rejections not set forth below have been withdrawn.

Claim Objections

Claim 35 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). In the interest of compact prosecution, claim 35 is examined as though it comprises the transgene of claim 27. Appropriate correction is required.

Claim Rejections - 35 USC § 112

Claims 23-31 and 33-46 are rejected, under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection. Currently amended claims 23-31 and newly

added claims 41-46 recite the limitations "plant E2F protein", "plant DP protein", "plant E2F transgene", "plant DP transgene", "native E2F gene", "native DP gene", "heterologous E2F gene", heterologous DP gene", "E2F transgene" and "DP transgene". These limitations do not find support in the specification as filed and thus constitute new matter. Dependent claims 33-40 are included in the rejection.

Claims 23-31 and 33-39 remain rejected, and claims 40-46 are rejected, under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the office action mailed June 3, 2003.

Applicant's arguments filed December 8, 2003 have been fully considered but they are not persuasive.

Applicant argues that the rejection should be withdrawn in light of the amendment of claims 23, 24, 27 and 28 to recite that the plant cells are transformed with coding sequences for "a plant E2F protein" and "a plant DP protein", wherein the proteins form part of an E2F/DP heterodimeric transcription factor involved in the regulation of G1/S transition of the cell cycle (reply pages 10-11).

The rejection is maintained because the specification does not describe a representative number of species of plant E2F and DP transgenes and proteins, or the structural features of plant E2F and DP transgenes and proteins unique to this genus. The genus "plant E2F and DP

transgenes and proteins" encompasses all E2F and DP transgenes and proteins from all plant species in the plant kingdom, a kingdom of organisms that by one estimate contains as many as 500,000 species (see for example Brown, Science, 13 August 1999, Vol. 285, No. 5430, pages 990-991, page 990 second paragraph, discussing "Eve", the mother of all 500,000 green plant species). In contrast, the specification describes E2F sequences from only four plant species, as well as two full-length DP sequences from a single plant species and partial DP sequences from three plant species. Furthermore, only one E2F sequence and one DP sequence are characterized as functioning to increase ploidy and modulate endoreduplication in plant cells. Additionally, rejected claims 23-31, 33-39 and 45-46 recite no structural limitations that distinguish plant E2F and DP transgenes and proteins from E2F and DP transgenes and proteins obtained from other organisms.

Furthermore, claim 31 and dependent claims 33-39, and newly added claims 41-44 are not limited to the use of plant E2F and DP transgenes and proteins, but encompass the use of any E2F and DP transgene and protein obtained from any source for the purpose of increasing ploidy and modulating endoreduplication in plant cells. The specification does not describe a representative number of species of this broad genus, or the structural features of E2F and DP transgenes and proteins unique to this genus. Additionally, rejected claims 41-44 recite no structural limitations that distinguish E2F and DP transgenes and proteins from other transgenes and proteins.

Claims 23-31 and 33-39 remain rejected, and claims 40-46 are rejected, under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for

increasing endoreduplication in plants by overexpressing an isolated nucleic acid corresponding to the *Arabidopsis* E2Fa gene, and a method of increasing endoreduplication in plants by overexpressing isolated nucleic acids corresponding to the *Arabidopsis* E2Fa and DPa genes, and a method of decreasing endoreduplication in cotyledon pavement cells and increasing endoreduplication in hypocotyl and cotyledon cortical and palisade cells and in mature trichome cells by overexpressing isolated nucleic acids corresponding to the *Arabidopsis* E2Fa and DPa genes, does not reasonably provide enablement for methods for modulating endoreduplication by transforming a plant cell with a coding sequence for an E2F or DP protein obtained from any species of organism, including any species of plant.. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims, for the reasons of record set forth in the office action mailed June 3, 2003.

Applicant's arguments filed December 8, 2003 have been fully considered but they are not persuasive.

Applicant argues that the rejection should be withdrawn as genes for other plant E2F and DP proteins were available at the time of filing, and one skilled in the art would reasonably believe that corresponding genes from other plant species would function similarly to the *Arabidopsis* E2Fa and DPa genes exemplified. Applicant points to the disclosure of E2F transgenes from tobacco, wheat, carrot and *Arabidopsis*, and the disclosure of two DP transgenes from *Arabidopsis*, as well as partial DP sequences from other plant DP genes from soybean, tomato and cotton deposited in genetic databases. Applicant additionally points to the cited reference of Albani et al., which discloses that the carrot E2F protein has 50% and 54%

homology to wheat and tobacco E2F proteins, that there is 75% amino acid sequence identity between the DNA-binding domains of tobacco, wheat and human E2F proteins, that the DP dimerization domain and marked box domain are also well conserved in plant E2F proteins, that the carrot E2F can transactivate an E2F reporter gene in both plant and mammalian cells, and that carrot E2F can bind the human DP protein in vivo. Applicant additionally submits that a plant genome does not comprise a multitude of E2F or DP sequences, as the *Arabidospsis* genome, for example contains only three E2F genes and two DP genes. (reply pages 11-13)

The rejection is maintained because the specification does not provide sufficient guidance for one skilled in the art to determine which E2F and DP transgenes would function to increase ploidy and modulate endoreduplication in plant cells and which would not. Such guidance is necessary because the effect of expressing different transgenes on ploidy and endoreduplication in plant cells is unpredictable. Absent such guidance one skilled in the art would have to resort to trial and error testing of each E2F and DP sequence to determine what effects, if any, each would have on ploidy and endoreduplication in plant cells. Such trial and error testing would constitute undue experimentation.

With respect to the availability at the time of filing of genes for other plant E2F and DP proteins, the Examiner maintains that the availability of E2F sequences from only four plant species, as well as two full-length DP sequences from a single plant species and partial DP sequences from three plant species does not provide sufficient guidance for which E2F and DP transgenes would function to increase ploidy and modulate endoreduplication in plant cells and which would not, as only one plant E2F and one plant DP sequence, each obtained from a single plant species (*Arabidopsis*) has been characterized as functioning to increase ploidy and

modulate endoreduplication in plant cells. With respect to whether corresponding genes from other plant species would function similarly to the *Arabidopsis* E2Fa and DPa genes exemplified, the Examiner maintains that differences observed between different known E2F and DP genes, as discussed at page 7 of the office action mailed June 3, 2003, raise the question of which E2F or DP gene, or which plant E2F or DP gene, could be substituted for the *Arabidopsis* E2Fa and DPa genes in order to increase ploidy and modulate endoreduplication in plant cells.

With respect to the cited reference of Albani et al., it is unclear the extent to which the observed structural conservation among three plant and one human E2F proteins provides guidance for the selection of E2F and DP transgenes for the purpose of increasing ploidy and modulating endoreduplication in plant cells, as only one plant E2F and one plant DP sequence, each obtained from a single plant species (*Arabidopsis*) has been characterized as having this function. It is also unclear the extent to which the observed functional compatibility of one carrot E2F protein and one human DP protein provides guidance for the selection of E2F and DP transgenes for the purpose of increasing ploidy and modulating endoreduplication in plant cells, as neither the carrot E2F protein nor the human DP protein has been characterized as having this function.

With respect to the enumeration of E2F or DP sequences, the Examiner does not dispute that the genome of a single plant species may contain only a limited number of E2F or DP sequences. In this regard it is noted that the rejected claims are not limited to E2F and DP sequences obtained from a single plant species. The rejected claims are directed to E2F and DP sequences obtained from all species of organisms, including all plant species. Either such genus

would encompass a multitude of E2F or DP sequences exhibiting structural and functional differences as well as similarities.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 23, 24, and 41-46, and claims 25-26 and 40 dependent thereon, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejected claims are indefinite because it is unclear how the coding sequence used to transform the cell operates to increase ploidy and modulate endoreduplication. Claims 23-24 and 45-46 merely recite that a plant cell is "transformed" with a coding sequence, without reference to what the coding sequence does. Claims 41-44 recite only that the transgenic plant "expresses" a transgene or transgene product, without reference to what type of transgene product is expressed.

Claim 31 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 31 is directed to the plant of claim 28 selected from plants having plant cells which express the products of native or heterologous EF2 and DP genes. Because the plant cells of claim 31 express the products of "a" native or heterologous "EF2 gene" and "a" native or heterologous "DP gene", it is unclear whether the expressed native and heterologous EF2 and DP genes of claim 31 correspond to "the plant E2F transgene" and "the plant DP transgene" in the plant cells of the plant of claim 28.

Claim Rejections - 35 USC § 103

Claim 29 remains rejected, and claims 23, 25, 27, 30, 33-39, and 41-44 are rejected, under 35 U.S.C. 103(a) as being unpatentable over Albani et al. (The Journal of Biological Chemistry, 23 June 2000, Vol. 275, No. 25, pages 19258-19267) in view of Ramirez-Parra et al. (Nucleic acids Research, 1999, Vol. 27, No. 17, pages 3527-3533), for the reasons of record set forth for claim 29 in the office action mailed June 3, 2003.

Applicant's arguments filed December 8, 2003 have been fully considered but they are not persuasive.

Applicant argues that there is no suggestion or motivation in Albani et al. or Ramirez-Parra et al. to produce a plant which stably expresses an E2F transgene. With respect to Albani et al., Applicant argues that there is no teaching or suggestion in Albani et al. for the stable transformation of a plant cell with a heterologous E2F transgene or for the regeneration of stably transformed plants, since Albani et al. carried out their transactivation experiments using carrot cells transformed with a homologous carrot E2F transgene, and since Albani et al. only transiently expressed the carrot E2F in carrot cells in order to test the carrot E2F for its ability to function in plant cells as a transcriptional activator. With respect to Ramirez-Parra et al., Applicant argues that there is no teaching or suggestion in Ramirez-Parra et al. for the stable transformation of a plant cell with a heterologous E2F transgene or for the regeneration of stably transformed plants, since Ramirez-Parra et al. teach only the isolation and cloning of a wheat cDNA encoding a protein which interacts with a plant RBR protein. Applicant argues that at most the combined teachings might provide an invitation to experiment, but they do not render the rejected claims obvious (reply pages 19-21).

The Examiner maintains that the rejected claims are obvious over Albani et al. in view of Ramirez-Parra et al. The combined teachings are not an invitation to experiment as the rejected claims merely require the production of plants that stably express a plant E2F transgene. The production of plants that stably express plant transgenes, including heterologous as well as homologous plant transgenes, was well within the abilities of one skilled in the art at the time of filing. Plant E2F transgenes were also known in the art at the time of filing, and it was further known that the amino acid sequences of the carrot, wheat (disclosed by Ramirez-Parra et al.) and tobacco E2F proteins are conserved in functionally significant regions such as the DNA binding domain and the DP dimerization domain (Albani et al., page 19261 column 1 last paragraph; page 19262 Figure 3). Motivation for the transformation of plants to study the role of E2F genes in plants is also provided by Albani et al., who disclose that transformation studies conducted in animals indicate that at least one animal E2F is dispensable for cell proliferation (page 19266, col. 2, top paragraph).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Remarks

No claim is allowed.

Claims 24, 26, 28, 31, 40 and 45-46 are deemed free of the prior art, due to the failure of the prior art to teach or suggest transgenic plants that coexpress recombinant E2F and DP proteins.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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